

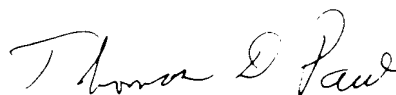
## REMARKS

Please substitute and examine the above-presented claims for those pending in the PCT application. The above-presented claims represent re-written claims of the PCT application in U.S. format. These amendments do not narrow the scope of the claims within the meaning of *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 234 F3d 558, 586, 56 USPQ2d 1865, 1886 (Fed. Cir. 2000). No new matter has been added by these amendments.

Applicants have attached a marked version of the claims in this application. Additionally, Applicants have attached a clean copy of all pending claims in this application after amendments.

Applicants address fees in the Fee Transmittal filed herewith. However, if Applicants owe any additional fees now or at any time during the prosecution of this application, please charge the deposit account of Fulbright & Jaworski, L.L.P., account number 06-2375, from which the undersigned is authorized to withdraw.

Respectfully submitted,



---

Thomas D. Paul  
Registration No. 32,714  
Counsel for Applicants

Date: 7/27/01  
Fulbright & Jaworski L.L.P.  
1301 McKinney, Suite 5100  
Houston, Texas 77010-3095  
Telephone: 713-651-5325  
Telecopier: 713-651-5246

25055328.1

Express Mail Label No.  
EK102656891US (7 27 01)

**MARKED VERSION OF CLAIMS SHOWING AMENDMENTS**

1. (Amended) A formulation for [use in] a therapeutic [and/] or a cosmetic treatment, which formulation comprises:

at least one anti-sense polynucleotide to a connexin protein[;] together with a pharmaceutically acceptable carrier or vehicle.

3. (Amended) A formulation according to claim 1 [or 2], wherein the polynucleotide is an oligodeoxynucleotide.

4. (Amended) A formulation according to [any preceding] claim 1 which contains polynucleotides to one connexin protein only.

6. (Amended) A formulation according to [any of] claim[s] 1 [to 3] which contains polynucleotides to more than one connexin protein.

9. (Amended) A formulation according to claim 5 [, claim 7 or claim 8] in which the polynucleotide to connexin 43 is selected from the group consisting of:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC;

GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC; and

GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT.

10. (Amended) A formulation according to claim 5 [or claim 8] in which the polynucleotide to connexin 26 is:

TCC TGA GCA ATA CCT AAC GAA CAA ATA.

11. (Amended) A formulation according to claim 5 [or claim 8] in which the polynucleotide to connexin 31.1 is:

CGT CCG AGC CCA GAA AGA TGA GGT C.

12. (Amended) A formulation according to claim 5 [or claim 8] in which the polynucleotide to connexin 32 is:

TTT CTT TTC TAT GTG CTG TTG GTG A.

13. (Amended) A formulation according to [any preceding] claim 1 in which the pharmaceutically acceptable carrier or vehicle is, or includes, a gel.

15. (Amended) A formulation according to [any preceding] claim 1 which further includes a surfactant or urea to assist with polynucleotide penetration into a cell[s].

16. (Amended) A method of site-specific downregulation of connexin protein expression for a therapeutic [and/] or a cosmetic purpose which comprises administering a formulation as defined in [any one of] claim[s] 1 [to 15] to a site on or within a patient at which said downregulation is required.

17. (Amended) A method of reducing neuronal cell death which would otherwise result from a neuronal insult to a specific site in the brain, spinal cord or optic nerve of a patient which comprises the step of administering a formulation as defined in [any one of] claim[s] 1 [to 15] to said site to downregulate expression of a connexin protein[(s)] at and immediately adjacent said site.

19. (Amended) A method according to claim 17 in which the formulation is administered in a sufficient amount to downregulate expression of said connexin protein[(s)] for at least 24 hours post-administration.

20. (Amended) A method of promoting wound healing in a patient which comprises the step of administering a formulation as defined in [any of] claim[s] 1 [to 15] to said wound to downregulate expression of a connexin protein[(s)] at and immediately adjacent the site of said wound.

23. (Amended) A method according to claim 20 in which the wound is the result of a surgery.

24. (Amended) A method of reducing inflammation as part of treating a wound [and/] or a tissue subjected to a physical trauma which comprises the step of administering a formulation as defined in [any one of] claim[s] 1 [to 15] to, or proximate to, said wound or tissue.

26. (Amended) A method of decreasing scar formation in a patient who has suffered a wound which comprises the step of administering a formulation as defined in [any one of] claim[s] 1 [to 15] to said wound to downregulate expression of a connexin protein[(s)] at and immediately adjacent the site of said wound.

27. (Amended) A method of skin rejuvenation or thickening for a cosmetic or a therapeutic purpose which comprises the step of administering, once or repeatedly, a formulation as defined in [any one of] claim[s] 1 [to 15] to a [the] skin surface.

30. (Amended) A method according to [any one of] claim[s] 27 [to 29] wherein said formulation is a cream.

**CLEAN COPY OF ALL PENDING CLAIMS AS OF JULY 27, 2001**

A<sup>1</sup>  
1. (Amended) A formulation for a therapeutic or a cosmetic treatment, which formulation comprises:

at least one anti-sense polynucleotide to a connexin protein together with a pharmaceutically acceptable carrier or vehicle.

2. A formulation according to claim 1, suitable for topical administration.

A<sup>2</sup>  
3. (Amended) A formulation according to claim 1, wherein the polynucleotide is an oligodeoxynucleotide.

4. (Amended) A formulation according to claim 1 which contains polynucleotides to one connexin protein only.

5. A formulation according to claim 4 wherein said connexin protein is connexin 43, connexin 26, connexin 31.1, connexin 32 or connexin 36.

A<sup>3</sup>  
6. (Amended) A formulation according to claim 1 which contains polynucleotides to more than one connexin protein.

7. A formulation according to claim 6 in which one of the connexin proteins to which polynucleotides are directed is connexin 43.

8. A formulation according to claim 6 which includes polynucleotides directed to at least two of connexin 26, connexin 31.1, connexin 32, connexin 36 and connexin 43.

9. (Amended) A formulation according to claim 5 in which the polynucleotide to connexin 43 is selected from the group consisting of:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC;  
GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC; and  
GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT.

10. (Amended) A formulation according to claim 5 in which the polynucleotide to connexin 26 is:

TCC TGA GCA ATA CCT AAC GAA CAA ATA.

11. (Amended) A formulation according to claim 5 in which the polynucleotide to connexin 31.1 is:

CGT CCG AGC CCA GAA AGA TGA GGT C.

12. (Amended) A formulation according to claim 5 in which the polynucleotide to connexin 32 is:

TTT CTT TTC TAT GTG CTG TTG GTG A.

13. (Amended) A formulation according to claim 1 in which the pharmaceutically acceptable carrier or vehicle is, or includes, a gel.

14. A formulation according to claim 13 in which the gel is a nonionic polyoxyethylene-polyoxypropylene copolymer gel.

15. (Amended) A formulation according to claim 1 which further includes a surfactant or urea to assist with polynucleotide penetration into a cell.

A<sup>5</sup>  
16. (Amended) A method of site-specific downregulation of connexin protein expression for a therapeutic or a cosmetic purpose which comprises administering a formulation as defined in claim 1 to a site on or within a patient at which said downregulation is required.

17. (Amended) A method of reducing neuronal cell death which would otherwise result from a neuronal insult to a specific site in the brain, spinal cord or optic nerve of a patient which comprises the step of administering a formulation as defined in claim 1 to said site to downregulate expression of a connexin protein at and immediately adjacent said site.

18. A method according to claim 17 in which the formulation is administered to reduce neuronal loss due to physical trauma to the brain, spinal cord or optic nerve.

A<sup>6</sup>  
19. (Amended) A method according to claim 17 in which the formulation is administered in a sufficient amount to downregulate expression of said connexin protein for at least 24 hours post-administration.

20. (Amended) A method of promoting wound healing in a patient which comprises the step of administering a formulation as defined in claim 1 to said wound to downregulate expression of a connexin protein at and immediately adjacent the site of said wound.

21. A method according to claim 20 in which the wound is the result of trauma.

22. A method according to claim 21 in which the trauma is a burn.

A<sup>7</sup>  
23. (Amended) A method according to claim 20 in which the wound is the result of a surgery.

A<sup>7</sup>  
24. (Amended) A method of reducing inflammation as part of treating a wound or a tissue subjected to a physical trauma which comprises the step of administering a formulation as defined in claim 1 to, or proximate to, said wound or tissue.

25. A method according to claim 24 in which the formulation is administered to reduce inflammation due to physical trauma to the brain, spinal cord or optic nerve.

A<sup>8</sup>  
26. (Amended) A method of decreasing scar formation in a patient who has suffered a wound which comprises the step of administering a formulation as defined in claim 1 to said wound to downregulate expression of a connexin protein at and immediately adjacent the site of said wound.

27. (Amended) A method of skin rejuvenation or thickening for a cosmetic or a therapeutic purpose which comprises the step of administering, once or repeatedly, a formulation as defined in claim 1 to a skin surface.

28. A method according to claim 27 wherein said formulation includes polynucleotide directed to connexin 43 and is administered to regulate epithelial basal cell division and growth.

29. A method according to claim 27 wherein said formulation includes polynucleotide directed to connexin 31.1 and is administered to regulate outer layer keratinisation.

A<sup>9</sup>  
30. (Amended) A method according to claim 27 wherein said formulation is a cream.

31. The use of at least one anti-sense polynucleotide to a connexin protein in the manufacture of a medicament for downregulating expression of said connexin protein for a therapeutic or cosmetic purpose.



32. The use of claim 31 wherein said medicament is for reducing neuronal cell death which would otherwise result from a neuronal insult.

33. The use of claim 31 wherein said medicament is for promoting wound healing.

34. The use of claim 31 wherein said medicament is for reducing inflammation.

35. The use of claim 31 wherein said medicament is for decreasing scar formation.

36. The use of claim 31 wherein said medicament is for skin rejuvenation for a cosmetic or therapeutic purpose.

37. A formulation according to claim 2, wherein the polynucleotide is an oligodeoxynucleotide.

38. A formulation according to claim 7 in which the polynucleotide to connexin 43 is selected from the group consisting of:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC;  
GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC; and  
GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT.

39. A formulation according to claim 8 in which the polynucleotide to connexin 43 is selected from the group consisting of:

GTA ATT GCG GCA AGA AGA ATT GTT TCT GTC;  
GTA ATT GCG GCA GGA GGA ATT GTT TCT GTC; and  
GGC AAG AGA CAC CAA AGA CAC TAC CAG CAT.

40. A formulation according to claim 8 in which the polynucleotide to connexin 26 is:

TCC TGA GCA ATA CCT AAC GAA CAA ATA.

41. A formulation according to claim 8 in which the polynucleotide to connexin 31.1 is:

CGT CCG AGC CCA GAA AGA TGA GGT C.

42. A formulation according to claim 8 in which the polynucleotide to connexin 32 is:

TTT CTT TTC TAT GTG CTG TTG GTG A.